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The Implications of Male Circumcision on HIV Transmission

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Senior Thesis

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Abstract:

Human immunodeficiency virus (HIV) is one of the world's biggest health threats. In 2010, 33.3 million adults and children were predicted to be living with HIV/AIDS. Although prevention methods such as abstinence, condoms, and fewer sexual partners will help to lower the number of people infected by HIV, they are not enough. Male circumcision may provide an extra prevention method to acquiring HIV. A correlation between male circumcision and HIV transmission was first discovered in areas in western and northern Africa where the male circumcision prevalence rates tend to be high and HIV prevalence tends to be low. The foreskin of the penis remains largely unkeratinized and thus more prone to microtrauma, tears, and ulcers which could increase the transmission of HIV. The foreskin also plays host to a high concentration of langerhans cells which have been shown to increase HIV transmission. Langerhans cells, which generally aid in immune responses to invading pathogens can bind HIV at a specific receptor site and deliver it to the lymph nodes. The HIV will then proliferate throughout the body. Studies show that male circumcision has the potential to decrease female to male transmission of HIV by 60%. Through mathematical modeling, case studies, and statistical analyses, it was found that male circumcision programs will be effective in lowering HIV incidence, prevalence, and death rates. The acceptability of a male circumcision program is relatively high in Sub-Saharan Africa and most specifically in Southern Africa, which has the highest HIV prevalence rates in the world. The cost-effectiveness and possible mass circumcision program implementation were also examined and found to be positive influences. Male circumcision although useful in preventing HIV, must be used in conjunction only with other HIV prevention methods.

The Implications of Male Circumcision on HIV Transmission

AliciaMarie V. Hurlburt

Introduction:

According to the World Health Organization, HIV or human immunodeficiency virus, is a serious threat to human life around the world (2009, 7). The organization states that HIV poses the biggest threat to regions of Sub-Saharan Africa (WHO, 2009, 7). The 2007 WHO update on the HIV/AIDS epidemiological surveillance report in the African region, reports that Botswana, a stable country in Southern Africa, has the second highest HIV prevalence rate in the world (2008, 27). One in every four people in the country has HIV (WHO Regional Office of Africa, 2008, 27). This number is astounding, and despite the government's attempts to implement successful treatment programs there has been very little decrease in HIV prevalence or incidence. In the Fall of 2010 I had the amazing opportunity to study abroad in Botswana and observe firsthand the impact that HIV has on the country. Every person I met in Botswana, from those living in the urban town to the people in the rural villages, was in some way affected by the HIV epidemic. In many cases, family members had been lost and in some instances a loss of livelihood ensued. As part of my schooling while abroad, I worked in urban and rural health clinics. While working in an ARV clinic, I saw hundreds of Botswana suffering from HIV. Some people were controlling the disease well with treatment, while others were neglectful of treatment and behavior. The staff at the clinic agreed that the government's ability to give free treatment to its citizens was important, but that it simply wasn't enough.

When I was in Botswana, I enjoyed learning about a country that I knew very little about. Since HIV has such an impact on the people there, I did a lot of research on the disease and treatments for it. In my studying, I came across the idea of male circumcision as a method to decrease the risk of HIV transmission. If this method proves to be effective in lowering the transmission of HIV, many lives can be saved. Male circumcision is a delicate subject in many areas of Sub-Saharan Africa due to the varied religious and cultural views. However, if it is a substantial method to lowering the rate of HIV then it should be investigated. To determine if such a male circumcision program will be feasible, it is important to look at the connection between male circumcision and HIV in terms of history, biology, and social aspects.

Brief History of Male Circumcision:

In 2009, the World Health Organization estimated that 30% of all males above the age of 15 are circumcised globally (WHO, 2009, 6).

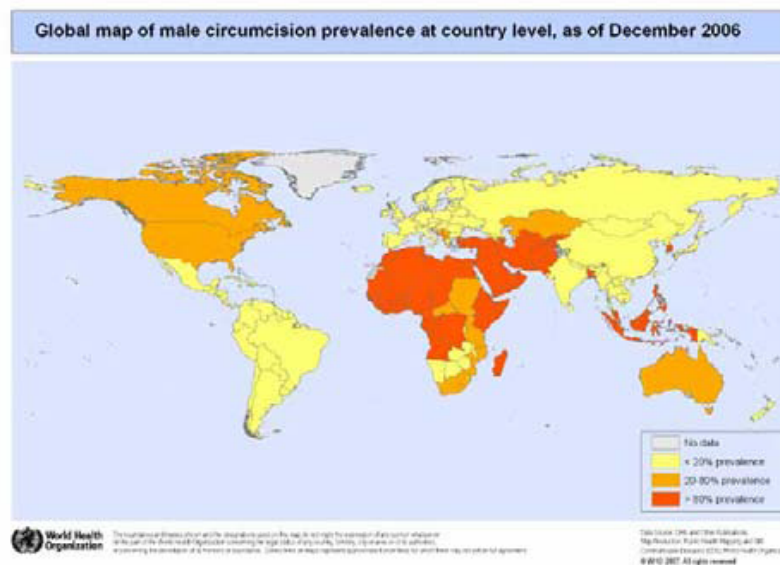


FIGURE 1: Geographic Distribution of Male Circumcision as of December 2006.
World Health Organization, 2009.

There is much debate between anthropologists over the time origins of male circumcision. Some believe that male circumcision began in one particular region of the world. The exact place is unknown; however, Egypt is generally accepted as the place of origin. It is assumed that it moved gradually from one community to others more than 15,000 years ago (WHO, 2009,14). Other anthropologists state that male circumcision developed independently with different cultures (WHO, 2009,14). The earliest evidence of male circumcision can be traced to ancient Egyptian dynasties. A depiction of male circumcision on the sarcophagus of Ankh-ma-Hor during Egypt's sixth dynasty (2600 BCE) suggests that it was a precursor to entering the priesthood (Aggleton and Thomas, 2007). In this regard, male circumcision was used as a tool to induce purity among men. The removal of the foreskin in ancient Egypt was thought to act as a cleansing tool that corrected the natural flow of the body (Gollaher, 2000, 5).

Between 2000 and 1800 BCE, male circumcision took on a more widespread role in religion. During the life of Abraham, God said "Every male among you shall be circumcised. You shall be circumcised in the flesh of your foreskins, and it shall be a sign of the covenant between me and you" (Genesis 17:10-11). Circumcision at this time was used as a tool to bring one closer to God. Because the command to circumcise was given by God, the act of doing so implied that one was devoted to Him. The bond between "the maker" and "the children" was thus enforced through obedience.

Through the years, male circumcision has been used as a means to induce purity, strengthen the relationship with God, and as a way to progress to manhood (Aggleton and Thomas, 2007). In a review of male circumcision, Aggleton and Thomas discuss its use to punish, hurt others, and to cure ailments and made-up diseases (2007). The same review also

describes male circumcision from a political perspective when it was used during Nazi Germany and the Armenian genocide to impose power and social order over others (Aggleton and Thomas, 2007). During these times, circumcision status was often used as a means to determine if someone would be condemned to death or allowed to live. Males of all ages were forcibly circumcised during the Armenian genocide while torture and death were often the consequences for those who were uncircumcised in Nazi Germany and during the Ottoman and Moorish Empires (Aggleton and Thomas, 2007). In Sub-Saharan Africa, where 28 of 45 countries exceed 80% of male circumcision prevalence, circumcision is carried out for cultural reasons (WHO, 2009, 6-15). It can symbolize movement into manhood, masculinity, initiation rites, a blood sacrifice to the ancestors of the earth, or it may be used as a social construct to engage in relationships with women (Paise, 1978; WHO, 2009, 6-15).

The United States offers an interesting look at the origins of male circumcision. Although it was in some cases affected by religion; circumcision was justified during the 19th and early 20th centuries as a means to stop masturbation, cure mental illness, neurotic behaviors, and even adolescent rebellion (Paise, 1978). According to Paise, in the 1890s, many people in the US believed that masturbation could cause insanity and mental retardation (1978). Circumcision was therefore frequently used as a method to treat and prevent ‘masturbations insanity’ (Paise, 1978). Even after the fear of ‘masturbation insanity’ receded, people began believing that male circumcision could cure penile cancer, as a result of inaccurate studies. This theory, which was founded on the idea that all of the uncircumcised men in a cancer trial did not have penile cancer, was soon disproved and the rate of male circumcision seemed to stabilize by the 1950s and 60s (Paise, 1978). Paise notes that circumcision survives in regions where it is recommended by

healthcare professionals as a means of hygiene (1978). Circumcision also thrives where it has a religious or cultural tradition, as in Jewish and Arab nations, as well some tribes in Sub-Saharan Africa (Paise, 1978).

Male circumcision is defined as the surgical removal of some or all of the foreskin of the penis. Aside from the religious and cultural aspects of male circumcision it has become an important means of maintaining good health and hygiene. Uncircumcised men have been associated with higher rates of genital ulcers, urinary tract infections in infants, penile cancer, cervical cancer in female partners, and the transmission of human papillomavirus to women. In a study of 2,298 uncircumcised men in India it was found that uncircumcised men were more likely to have a genital ulcer at the baseline appointment (30.6% vs 22.0%, $p=0.0163$) and at the scheduled follow-up visits (6.7% vs 3.0% of visits, $p=0.0024$) than circumcised men (Reynolds, *et al.* 2004).

There is no concrete evidence that suggests a reason for the invention of male circumcision. Recently, research has pointed towards a positive correlation between male circumcision and HIV prevention. Studies have since shown that in areas where male circumcision is regularly practiced, the HIV prevalence rate tends to be relatively low (figure 3). Numerous mathematical models have been created and some show the potential of male circumcision to reduce HIV transmission from female to male by 60% (Williams, *et al.* 2006).

Brief History of HIV:

HIV-1 was officially discovered in the United States in 1984, just three years after reports of the first AIDS-like symptoms surfaced (Bellenir, 1998, 33). In 1986, scientists discovered

another strain of HIV (HIV-2), isolated mainly to areas within Western Africa. (Bellenir, 1998,34). HIV-1 is thought to have arisen via a cross species transmission between chimpanzees and humans, while HIV-2 may have occurred via a cross species transmission of a sooty mangabey virus (Cohen, *et al.* 2008). HIV-1 and HIV-2 can both ultimately cause AIDS, however HIV-2 immunodeficiency seems to develop more slowly and tends to be milder than an HIV-1 infection. HIV-2 infections have also been found to be less infective in the course of its early stages (Bellenir, 1998, p33-34). Most of the studies performed to assess the correlation between male circumcision and HIV prevention have been performed with HIV-1 (Baeten *et al.*, 2005; Cohen, *et al.*, 2008; de Jong, *et al.*, 2008; Kawamura, *et al.*, 2005; Reynolds *et al.*, 2005). Little is known about the association of male circumcision and HIV-2 infection. One study indirectly shows that male circumcision may decrease HIV-2 prevalence by linking the virus to higher rates of genital ulcers and STIs (Pepin, *et al.*, 1992). Because circumcision has been shown to decrease the risk of developing genital ulcers and STIs (Reynolds, *et al.*, 2004), circumcision practices may also help to decrease HIV-2 transmission.

The 2010 UN Global Report on AIDS stated that 33.3 million adults and children are currently living with HIV (UNAIDS, 2010). In less than thirty years, HIV moved from a single report of an infection cluster to a worldwide pandemic (Cohen, *et al.* 2008). In 2009, there were 2.6 million newly HIV infected adults and children since 2001, and that year 1.8 million deaths were related to AIDS (UNAIDS, 2010). Notably, Sub-Saharan Africa has 68% of the global HIV incidence and prevalence rates, 76% of global AIDS mortality rates, and 90% of the global HIV burden in children. (Zachariah, *et al.* 2010).

HIV functions to gradually destroy the immune system by killing or impairing its cells. It can be transmitted through sexual contact with an infected person, through infected blood (such as sharing needles with an infected person), or rarely through infected blood transfusions. HIV may also be passed from mother to child during birth or through breast milk (Bellenir, 1998, 3-11). During heterosexual sexual intercourse, HIV has three main pathways of crossing over the mucosal epithelium. The first pathway involves the trans-epithelial migration of langerhans cells that have just been infected with HIV. The virus may infect the host by a second pathway in which it penetrates across the epithelium into the lamina propria. Lastly, the virus may undergo transcytosis by the epithelial cells that it comes into contact with (Kawamura, *et al*, 2005).

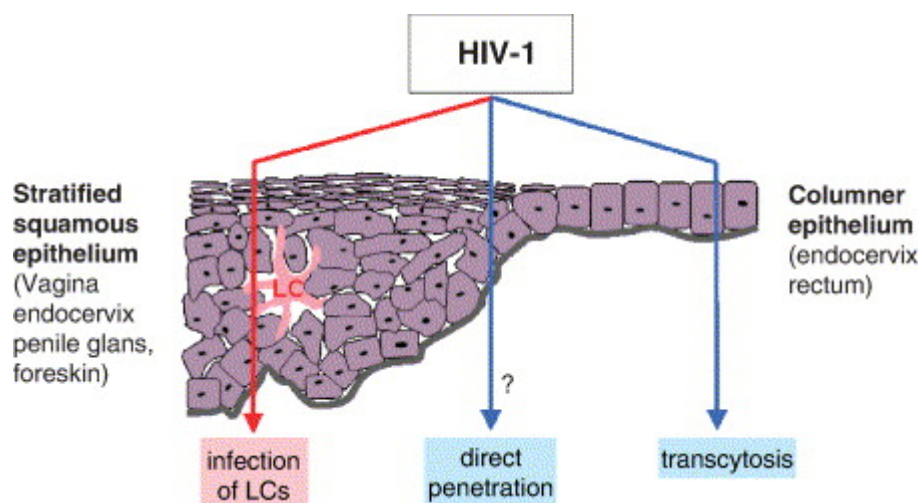


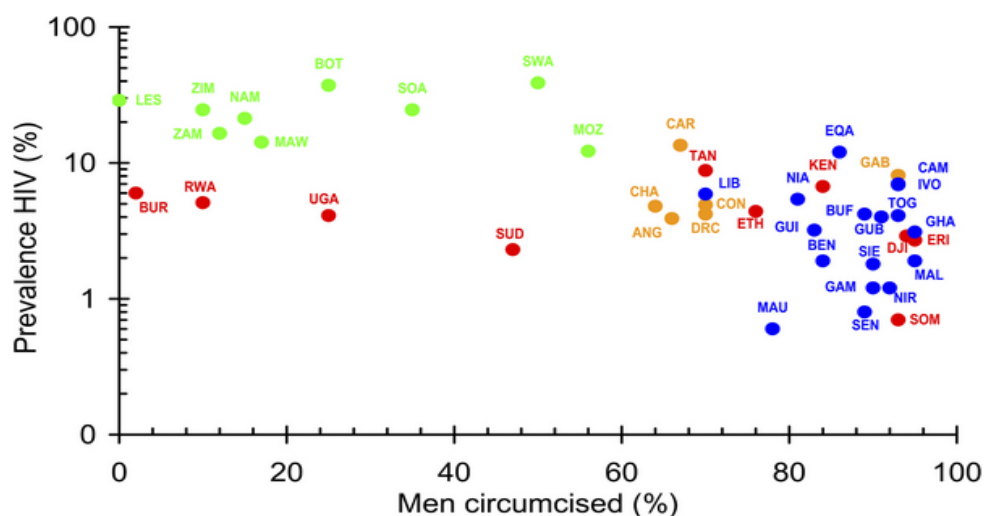
FIGURE 2: Three Main Pathways of HIV Transmission during Heterosexual Intercourse (kawamura, *et al*, 2005).

Since the discovery of HIV, governments, scientists, and populations have worked hard to eradicate the disease. The World Health Organization provides information on the many programs implemented to pave the way for a significant decrease in the number of people infected with HIV (WHO, 2011). The most obvious mode of HIV prevention is abstinence,

however condoms will aid in prevention if abstinence is not followed. Zacchariah, *et al* (2010) states that anti-retroviral therapy (ARV) was developed as a combination of drugs to repress the virus and prolong life. The published article states that for every person placed on this therapy, four to six more acquire the virus. In Sub-Saharan Africa, where ARV treatment is most needed, it was found that 7 out of 10 people who need the treatment are not receiving it (Zacchariah, *et al.* 2010). Although ARVs are helping to decrease the incidence, prevalence and mortality rates of HIV, more programs are needed to guarantee its eventual eradication.

The Correlation between Male Circumcision and HIV Transmission is Discovered:

Male circumcision is performed in many areas of Sub-Saharan Africa as a tribal rite of passage (Paise, 1978). It was in these circumcised populations, that researchers began to notice fewer cases of HIV/AIDS than in populations that did not circumcise males. These recorded findings serve as preliminary data pointing towards a positive correlation of estimated prevalence of male circumcision and prevalence of HIV (Williams, *et al.* 2006).



A positive correlation between male circumcision and HIV has also been observed and recorded in South and Southeast Asia. In countries where less than 20% of the male population is circumcised, there are higher rates of HIV seroprevalence (Table 1). However, in countries in which more than 80% of the male population is circumcised the HIV prevalence rates are drastically lower (Halperin and Bailey, 1999).

TABLE 1: Seroprevalence of HIV in South/Southeast Asian Countries by Estimated Proportion of Men Circumcised (Halperin and Bailey, 1999).

South and southeast Asia

<20% circumcised	Seroprevalence	>80% circumcised	Seroprevalence
Cambodia	2.40	Pakistan	0.09
Thailand	2.23	Philippines	0.06
Myanmar	1.79	Indonesia	0.05
India	0.82	Bangladesh	0.03
Nepal	0.24		

Biological Aspects of Male Circumcision and HIV Transmission:

As it has been clearly demonstrated that male circumcision and HIV prevalence rates have a positive correlation, the next thing to examine is the biology behind the protection that circumcision provides. During sexual intercourse, it is possible that an uncircumcised male may become infected from an HIV positive female via a genital ulceration present on the foreskin. It has been shown that an uncircumcised male will be more likely to contract an STI, such as Chlamydia, over a circumcised male. Having an STI increases the risk of HIV and therefore serves to support that uncircumcised males have higher prevalence rates of HIV (Reynolds, *et al.* 2004).

Langerhans cells may perhaps be the most influential link between the association of male circumcision and HIV. Kawamura *et al* (2005) describes Langerhans cells (LC) as being found specifically on the genitals of both men and women. The article states that in women LCs can be found in the mucosal epithelium of the vagina and in the extocervix. In men LCs are found in the glans penis and inner foreskin (Kawamura, *et al*, 2005). Langerhans cells, found among stratified squamous mucosal epithelial cells, are motile. Once these cells come into contact with an antigen they migrate from the epithelial tissue to the lymph nodes (Kawamura, *et al*, 2005). LCs are important in initiating an immune response to an invading pathogen. Once a pathogen is detected the LCs migrate from the epithelia to the lymph nodes where they present the antigen to T cells. The T cells are then responsible for inducing a primary immune response (Kawamura, *et al*, 2005).

HIV infection occurs mainly through antigen binding to CD4 and CCR5 receptors. Such receptors can be found on macrophages, langerhans cells, and dendritic cells in both the genital and rectal mucosa (Szabo and Shorth, 2000). HIV infection has been associated with the maturation of the Langerhans cells. Immature LCs express surface CCR5 receptors which play a crucial role in binding to the HIV. The immature LCs recognize HIV as an invading pathogen and allows it to bind to the CCR5 receptor. The cells then move to the lymph nodes, maturing in the process. Once in the lymph nodes, the LCs can pass the HIV to the CD4+ T cells, where the virus will begin to replicate and destroy the immune system (Kawamura, *et al*, 2005).

One study, performed by de Jong *et al*, in 2008, argues that Langerhans cells are inefficient in transmitting HIV and instead may help to protect against it. The study speaks specifically about the ability of Langerhans cells to express a C-type lectin called langerin. It is

shown by de Jong and his colleagues that langerin functions to capture the HIV and sufficiently degrade the virus to prevent infection (de Jong, *et al*, 2008). The authors of the study also found however, that genital coinfection could activate Langerhans cells to induce HIV transmission. High viral concentrations saturate the langerin that is expressed by the Langerhans cells, thus making it unable to degrade the HIV. De Jong *et al* created an ex-vivo skin explant model to study the correlation (2008). They found that bacterial or fungal pathogens causing coinfections activate Langerhans cells through TLR triggering. The TLR agonists were shown to induce the production of TNF- α , which along with the TLR1/TLR2 ligand, Pam3CysSerLys4 (Pam3CSK4), were shown to enhance HIV transmission through the Langerhans cells. TNF- α specifically increases the replication of HIV within the Langerhans cells, while Pam3CKS4 enhances the capture of the HIV(de Jong, *et al*, 2008). This study not only supports the idea that Langerhans cells play an important role in transmitting HIV, but also that coinfection and genital inflammation significantly increases the transmission of HIV (de Jong, *et al*, 2008).

Another study shows that specific microbiota on the foreskin may serve to induce HIV transmission via the Langerhans cells (Price, *et al*, 2010). The penile microbiota in 12 HIV negative men was examined both before and after circumcision in Uganda by Price and colleagues (2010). Forty-two different bacterial families were classified, and Pseudomonadaceae and Oxalobacteriaceae were the most abundant irrespective of circumcision status (Price, *et al*, 2010). The authors of the study showed that circumcision was associated with a significant change in the microbiota and a decrease in anaerobic putative microbiota bacterial families. They concluded that a microenvironment that was anoxic on the subpreputial space may support pro-inflammatory anaerobes that may activate Langerhans cells to present HIV to CD4 cells in

draining lymph nodes. They were therefore able to show that the reduction in putative anaerobic bacteria after circumcision may play a role in protection from HIV and other sexually transmitted diseases (Price, *et al* 2010).

A Closer Look at Male Circumcision and HIV Transmission:

Male circumcision, if universally implemented will have a significant impact on populations. The majority of research on the matter has been performed on the basis that male circumcision will reduce the risk of HIV transmission from female to male (Baeten, *et al*, 2005; Kawamura, *et al*, 2005; Szabo and Short, 2010) . Decreasing HIV infection among men will indirectly benefit women through an overall lower incidence rate of HIV (Williams, *et al*, 2006). Mathematical models can be used to assess the impact of male circumcision at a realistic population level. In one study models showed that 100% coverage of male circumcision, implemented in 2008, in Kisumu, Kenya and Rakai, Uganda would lower the HIV prevalence rate by 19% and 14% respectively, by 2020. The study also showed that there would be a substantial decrease in HIV prevalence among females. Within a few years of universal circumcision, it was expected that there would be a substantial reduction in prevalence of about 8% in Kisumu and 4% in Rakai (Allsalaq, *et al*, 2009).

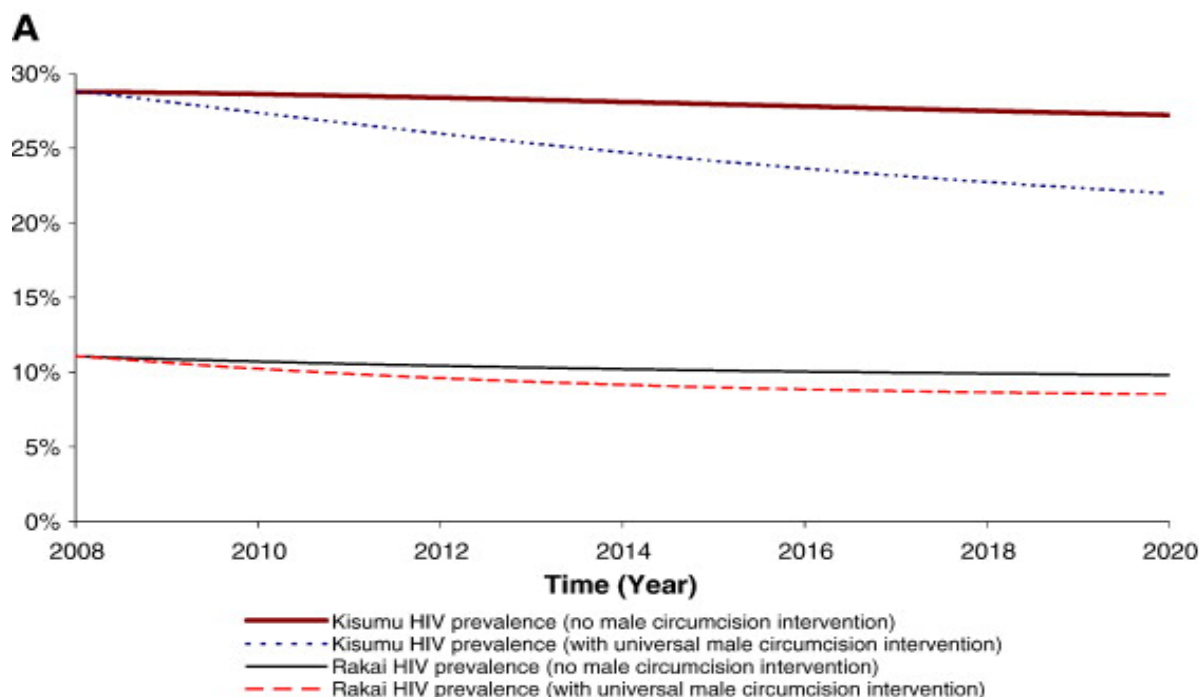


FIGURE 4: Impact of 100% Male Circumcision Coverage on HIV Prevalence in Kisumu, Kenya, and Rakai, Uganda. (Allsalaq, *et al*, 2009).

An HIV infected man is about two times as likely, per each contact, to infect a previously uninfected female partner, than an HIV infected woman is to infect a male partner (Williams, *et al*, 2006). The effects of male circumcision on HIV transmission from male to female are very much unknown. A study conducted by Turner *et al* in 2007 focused on a group of HIV negative women between the ages of 18 and 35 in Uganda and Zimbabwe. Every 12 weeks for 28 months, the women underwent extensive interviews about sexual practices, HIV status, contraceptive use, and partner status. They also gave specimen samples and underwent physical exams. Statistical analyses were performed to assess the effectiveness of male circumcision. The authors found that there is a suggestion of lower HIV risk for women with circumcised partners. In a subgroup designated as high-risk, the non-significant association is based on few HIV infections (19 total infections, with only two among the group of women with

circumcised partners). Because of the low number of infections in this high-risk group, male circumcision must be interpreted carefully as a cause of decreased HIV transmission (Turner, Morrison, and Padian, 2007).

Another study conducted in Rakai, Uganda argues the opposite of the previous study. A randomized control trial, funded by the Bill and Melinda Gates Foundation, was performed on 922 HIV positive males in Uganda (Wawer, *et al*, 2009). Some of these male participants were chosen to have either immediate circumcision or delayed (after 24 months) circumcision. HIV-negative female partners for each man were checked for HIV acquisition at 6, 12, and 24 months. Although the trial was terminated early due to futility, the researchers concluded that male circumcision did not prevent male to female transmission of HIV. HIV transmission may have even increased in cases where sexual intercourse resumed before the surgical wound was fully healed. This study however, did not look at the long-term effects of a male circumcision program and instead focused only on the intermediate effects (Wawer, *et al*, 2009).

Women may benefit from male circumcision because it has been known to decrease penile infections in males (Hankins, 2007). Such a decrease in infections and STIs will ultimately reduce the risk of female STIs and infections. It has also been found in some studies that women have a lower risk of developing cervical cancer if their partner is circumcised. As a means of HIV prevention, male circumcision should only be used as an additional preventative measure and must be undertaken with other appropriate precautions. If male circumcision becomes more widespread there is no doubt that women will benefit in the long-term; however it is important that other prevention methods, such as condoms, non-penetrative sex, and microbicides be used to decrease the risk of HIV infection in women.(Hankins, 2007).

Although heterosexual intercourse accounts for the majority of HIV acquisition in most areas of the world, HIV can also be transmitted from male to male through anal sex (UNAIDS, 2010). The effect of male circumcision on male to male HIV transmission is therefore an interesting subject which has been researched less extensively. Male to male anal sex can be broken down to two categories: insertive and receptive. The anal mucosa proves to be highly susceptible to trauma and will therefore greatly increase the risk of HIV infection during receptive sex. In insertive sex however, male circumcision may play a role in reducing the number of HIV target sites, specifically the Langerhans cells and macrophages. It is possible that male circumcision may be a useful tool in lowering the transmission of HIV from male to male in insertive sex practices only. More research needs to be done on the subject however, before any conclusions can be made (Ruan, *et al*, 2009).

Through the examination of many studies, I shown that male circumcision can be a useful tool in lowering the HIV transmission rate. An all-encompassing study, by Williams, *et al* showed that there could be a 60% decrease in female to male HIV transmission with the implementation of a male circumcision program in Sub-Saharan Africa (2006). The randomized control trial study which was funded by an NIH-NIDA grant, acts as conclusive evidence that male circumcision will work to fight against HIV. The study sought to estimate the potential impact of male circumcision on HIV incidence, prevalence, and death rates. Using parameter estimates for South Africa and extrapolating them to other countries, a mathematical model was developed. The potential for reduction of HIV transmission was found to be the greatest in Southern Africa, where the HIV prevalence rates are the highest. 174,000 new infections every year could be avoided just by increasing male circumcision in this region. It was concluded from

the study that from 2005-2025, male circumcision in Sub-Saharan Africa could avoid 5.7 new cases, 30 million deaths, and reduce the total number of people infected with HIV by 4.1 million (Williams, *et al*, 2006).

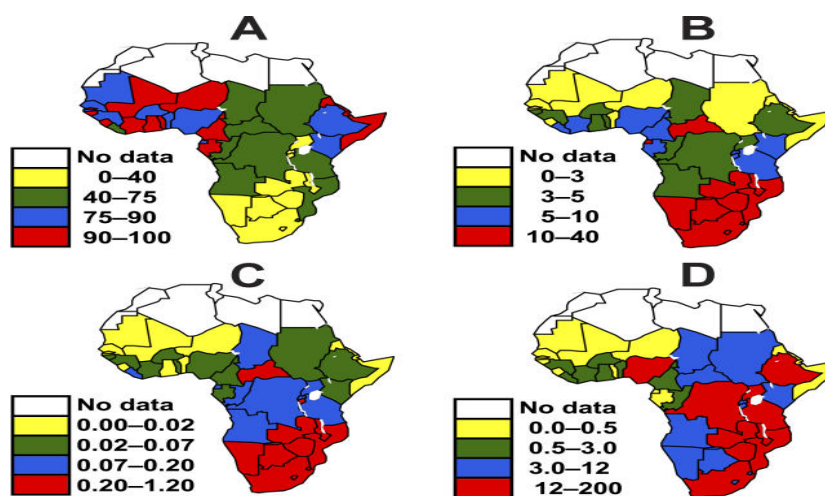


FIGURE 5: The Geographical Distribution of MC, HIV Prevalence, and the Potential Reduction in HIV Incidence if All Men Were Circumcised

(A) Proportion of men who are circumcised, χ (%).

(B) Prevalence of HIV in 2003, P (%).

(C) Potential impact of MC on the incidence of HIV infection, (% per year)

(D) Potential reduction in the number of new adult infections each year (thousands per year)

(Williams, *et al*, 2006).

Acceptability of Male Circumcision for Prevention of HIV:

Although more research would need to be carried out to assess the effects of male circumcision on age-specific populations, and in certain high-risk HIV areas, the implementation of a program has great potential to decrease the risk of HIV transmission. Knowing the biology behind the male circumcision and HIV association is a crucial step in implementing a circumcision program. The social aspects of male circumcision as a means of HIV prevention must also be explored. The acceptability of a male circumcision program in correlation with how

it fits in to a country's religion and culture are important factors that can be examined. Through a series of case-studies it is possible to show that the idea of male circumcision as a means to decrease HIV prevalence rate is generally well accepted.

A cross-sectional study across the country of Botswana, where the majority of the population is uncircumcised, was performed by the Botswana-Harvard AIDS Institute Partnership in 2001 (Kebaabetswe, *et al*, 2003). The researchers conducted interviews via a questionnaire form both before and after an informational pamphlet was read. The pamphlet appropriately described the advantages and disadvantages of male circumcision. The average age of the 605 people surveyed was 29. There was close to an equal representation of males and females and about 29 different ethnic groups were involved. Before hearing about the risks and benefits of male circumcision 68% of the people interviewed responded that they would “definitely or probably circumcise a male child if circumcision was offered free of charge and in a hospital setting”. After listening to the information, the percentage of people receptive to male circumcision for their male children was raised to 89%. There were 238 men in the study who claimed to be uncircumcised. 61% before the informational session, and 81% afterwards, said that they would undergo circumcision if it was offered free of charge and in a hospital setting. The study also sought to find out the best age and setting for male circumcision to occur. They found that more than half (55%) of the participants said the ideal age for circumcision was before six years. More than 90% of the people interviewed agreed that male circumcision should be performed in a hospital setting. The study therefore concluded with much supporting evidence that male circumcision would be widely supported in Botswana (Kebaabetswe, *et al*, 2003).

Sub-Saharan African countries have the highest HIV prevalence rates in the world, and it is in this region that male circumcision programs would help to decrease the spread of HIV most significantly and efficiently. However, with hundreds of tribal religions and cultures, the question of acceptability must be explored. Westercamp and Bailey (2007) performed a review of previous studies assessing the acceptability of male circumcision within individual countries in Sub-Saharan Africa. They pooled data from 13 specific studies in nine different countries, and were able to extrapolate numbers that would apply to all of Sub-Saharan Africa. The authors found that a median of 65% (range 29-87%) of uncircumcised men were willing to become circumcised. Sixty nine percent (47–79%) of women preferred circumcision for their partners, and 71% (50–90%) of men and 81% (70–90%) of women would circumcise their sons if given the chance (Westercamp and Bailey, 2007).

The male circumcision review study by Westercamp and Bailey (2007) sought to name some of the main facilitators of the acceptability of male circumcision as well as the most important barriers. Some of the noted barriers to male circumcision as a choice were found to be pain, culture and religion, cost, complications and adverse effects, and potential for behavior disinhibition. Many of the participants agreed that if male circumcision was to be promoted by the government than it should be available for free or at a reduced cost. Almost everyone within the 13 studies agreed that male circumcision would directly aid in penile hygiene. Many of the studies showed that people were aware that circumcision could provide protection from STIs and HIV. Participants expressed that it would be easier to see ulcers and rashes in a circumcised man and that the foreskin was often an entry place for STIs and other germs. Other important facilitators include the potential acceptability by other ethnic groups and sexual pleasure among

circumcised versus uncircumcised men. In South Africa, for example, it was found that men did not agree with the correlation between male circumcision and protection against STIs and HIV. Instead many men would undergo circumcision due to the belief that it would increase sexual pleasure. The authors of this review spoke of the need for information campaigns to precede male circumcision programs. These information campaigns would be tailored to address some of the common misconceptions about male circumcision. It was deemed that the acceptability of male circumcision in Sub-Saharan Africa was likely to be high enough that it will have a significant impact on the HIV prevalence rates throughout most of the continent (Westercamp and Bailey, 2007).

Male circumcision as a means of HIV prevention can be used in all areas of the world where HIV is a major health threat. In China, for example, more than 700,000 people were living with HIV at the end of 2007 (Ruan, *et al*, 2007). Approximately 11% of these people were thought to have contracted the virus through homosexual intercourse (Ruan, *et al*, 2007). Male circumcision is relatively rare in China. To assess the possibility of future intervention strategies, Ruan *et al* (2007) examined the willingness of homosexual men in China to be circumcised. In this study 328 homosexual men, found through advertising, out-reach programs and non-governmental AIDS agencies in Beijing, were involved in the study. Each man was interviewed individually after having read a pamphlet regarding male circumcision as a potential method to prevent HIV. Thirty-eight of the participants reported already being circumcised, most because of a tight foreskin, and six were unaware of their circumcision status. The analysis therefore only included the 238 participants who agreed to do the study. It was found that 81% of the participants said that male circumcision would be useful in maintaining hygiene. When asked if

they would undergo circumcision for AIDS research 123 of 238 males claimed that they would as long as it was a free medical procedure (Ruan, *et al*, 2007).

Although the US is not as severely threatened by HIV as Sub-Saharan Africa, it is interesting to look at male circumcision acceptability in the US for the purposes of future intervention techniques. Gust *et al* (2011) studied the acceptability of male circumcision as a means of HIV prevention as well as the possibility of risk compensation among patients in the US. The authors used a survey from 2008 in which it was asked of 20,000 men “how likely are you to get circumcised if your health care provider told you that circumcision would reduce your chance of becoming HIV infected”. The overall response rate was about half or 50.6%. A small percentage (13.1%) of uncircumcised men claimed that they would probably get circumcised if it would reduce HIV infection possibility. A total of 18% of the men responded in a way that noted a belief in risk compensation of circumcision. The study discussed the fact that the World Health Organization recommends male circumcision for countries or regions in which the prevalence rate of HIV exceeds 15%. The United States having a prevalence rate far lower than 15% (.6% in 2009 according to the 2010 UNAIDS report) does not need to consider a circumcision program now. However, the study did suggest that healthcare providers and specific groups should provide tailored educational material to teach the general public about the option of male circumcision as a means of HIV prevention (Gust, *et al*, 2011).

Male Circumcision as it Relates to Religion and Culture:

In 2007, it was estimated that 30% of all men in the world (or approximately 665 million) aged 15 years or older were circumcised (Hankins, 2007). Two-thirds of all circumcised men were Muslim. The Jewish population accounted for 0.8% of circumcised men, while 13%

were men living in the United States that were not categorized as Muslim or Jewish (Hankins, 2007). It is clear from the history of male circumcision that it has a religious and cultural meaning to many populations. The social aspects of circumcision as it relates to a specific religion are important to consider when constructing a male circumcision program to prevent HIV. Two case studies (Drain, *et al*, 2006; Reynolds, *et al*, 2004) will provide support and insight into the specificity of male circumcision as it relates to religion and culture.

Drain, *et al* (2007) published results in BMC Infectious Disease Journal, studied the relationship between male circumcision, Muslim and Christian religions, and seven infectious diseases in 118 developing countries. They used country specific data and a multivariate linear regression to show the association between circumcision and HIV in countries where the main mode of transmission was heterosexual intercourse. The study confirmed that male circumcision was associated with lower HIV prevalence and lower cervical cancer incidence. Drain *et al* used Sub-Saharan Africa as the variable for individual religions, and countries outside of Africa to control for religion. The authors suggested that for each categorical increase for male circumcision in Sub-Saharan Africa, there was a 1.84-fold decrease in the adult HIV prevalence. In non Sub-Saharan African countries, higher male circumcision prevalence was coupled with a 8.94-fold decrease in the adult HIV prevalence among countries with primarily heterosexual HIV transmission, but not among countries with mainly homosexual or injection drug use HIV transmission. Drain and colleagues concluded that independent of religion, male circumcision was associated with lower prevalence of HIV in Sub-Saharan Africa. It was also concluded that male circumcision closely correlates with religion. The authors determined that when a greater

percentage of the population is Muslim, there was a higher observed male circumcision prevalence rate, and vice versa for a majority of Christians (Drain, *et al*, 2006).

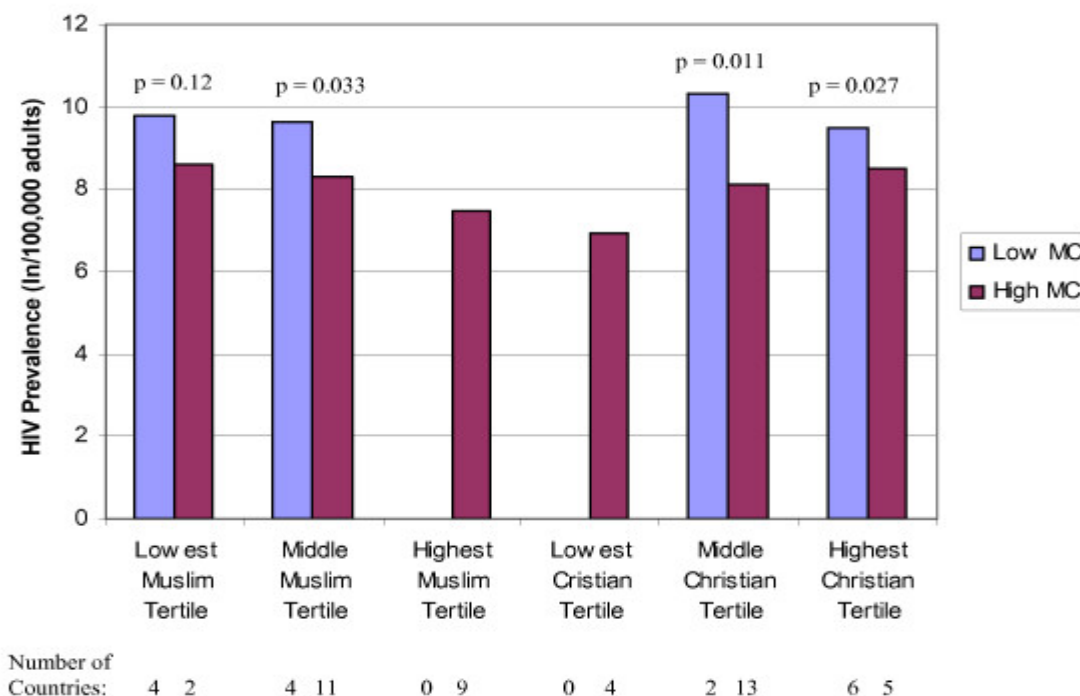


FIGURE 6: Natural log HIV prevalence (/100,000 adults) by low (<20%) and high (>80%) male circumcision (MC) prevalence and tertiles of the percent Muslim and Christian among 38 sub-Saharan African countries with primarily heterosexual HIV transmission.

In 2004, Reynolds and colleagues sought to describe the link between male circumcision and the risk of HIV-1 and other STIs in India. In their published article, Reynolds *et al* points out the clear association between circumcised men and religion. The subjects of the study included 2,298 HIV negative men attending sexually transmitted infection clinics in India between 1993 and 2000. The research was carried out by outlining the men's behavioral risk factors, STIs, and physical examinations to assess circumcision status. The study found that most circumcised men, (62.1%) identified themselves as Muslim, and most uncircumcised men (85.5%) identified

themselves as Hindu (Reynolds, *et al*, 2004). Although the study did not go much further into the link between religion and circumcision, it did highlight the main idea that religion and culture can and do affect prevalence of male circumcision. Religion may be a crucial determinant in the acceptability of male circumcision as a means to lower the risk of HIV transmission. Based on what is known about religion and its link to circumcision, education must be at the forefront of any male circumcision program.

Mass Circumcision and Cost Effectiveness of a Male Circumcision Program:

It has been shown that male circumcision will significantly decrease the incidence, prevalence, and ultimately death rates of HIV in areas where it is a major threat to human life. Moving forward now, the next step is to determine the feasibility, including possible methods, and cost effectiveness, of a male circumcision program.

Mass circumcision programs implemented in areas where HIV prevalence rate is high may help to lessen the global threat. One such program recruited 2013 infant, children, adolescents, and adult males for a circumcision procedure. Over a period of seven days, a disposable plastic clamp technique (figure 7) was employed to study the safety and efficiency of male circumcision. Each circumcision lasted on average 3.6 minutes. There was only a 2.47% complication rate, with the highest rate of complications among children younger than two years. Mass circumcision performed in this manner was found to be safe and time-saving. The average time for wound healing was 12.6 days for children younger than two years and 24.3 days for older ages. The study concluded overall that mass circumcision via a plastic clamp technique would be a beneficial and time-efficient method to circumcise a high number of males at any given age in any given population (Senel, *et al*, 2011).



FIGURE 7: Alisklamp used for mass circumcision study.

In Sub-Saharan Africa, where male circumcision may have the biggest impact, the cost effectiveness of circumcision programs is important to consider. A conclusive systematic review by Uthman *et al* (2010) examined five specific studies to determine the cost effectiveness of an adult male circumcision program versus no program for the prevention of heterosexual HIV acquisition among men in Sub-Saharan Africa. From all five studies looked at, it was found that the reported cost of each HIV infection averted could be between \$174 USD and \$2,808 USD. The authors therefore concluded that adult male circumcision programs in Sub-Saharan Africa could be cost-effective and in some cases even cost-saving (Uthman, *et al*, 2010).

Conclusion:

Male circumcision as a method to reduce the transmission of HIV has great potential. There are many studies that support the idea of a male circumcision program. Although religion and culture may act as deterrents, it has been suggested that education will help populations feel more settled (Klausner, *et al*, 2008). Country specific work will be the most crucial evidence to determine the acceptability, possibility, and cost-effectiveness of a mass male circumcision program. It has been shown by many of the stated studies, that such a program has the ability to save millions of lives. Male circumcision programs can be tested in areas that are most affected. Southern Africa will greatly benefit if the program can be correctly implemented.

It is critical that education go hand in hand with a male circumcision program. Male circumcision cannot stand alone and must be used in conjunction with other known HIV prevention techniques. Education about the procedure, healing time, and HIV in general are important. It is also important that the general public is educated on behavior and actions which are considered high-risk for HIV transmission.

When I was abroad I noticed a big flaw in the system to provide free ARV therapy to patients. Treatment for HIV had become so common that many people relied on it completely. Many people did not take the proper precautions to help prevent HIV, because it was known that they would receive free treatment that would help them live for a long time. Even while on treatment, some people thought that they could continue to have sex and spread the virus. There was certainly a lack of education about the treatment programs, however there was also a critical behavioral aspect that was missing. If the HIV epidemic is going to decrease, behavioral programs need to be implemented. Like the people of Botswana who rely on ARVs to keep them

alive and protect them against HIV, male circumcision might act as a similar net. It is concerning that men who are circumcised may think that they don't need to worry about contracting the HIV virus, when in fact it is still very possible. Male circumcision as a means to prevent HIV, is only one extra method that must be combined in a perfect balance with a multitude of other methods. Behavior, education, and understanding, along with male circumcision, ARV treatment, condoms, and abstinence will lessen the threat and may even eradicate HIV.

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